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CERTIFICATE OF HAND DELIVERY

I hereby certify that this paper is being delivered by hand to the U.S. Patent Office in accordance with 37 CFR § 1.6(b), addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231, on the date indicated.

Shirley Hall White

Name

March 4, 2002

Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of: L. Rambhatla et al.

Serial No.: 10/001,267

Filing Date: October 31, 2001

For: PROCESS FOR MAKING HEPATOCYTES  
FROM PLURIPOTENT STEM CELLS

Art Unit: 1632

Examiner: (unassigned)

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PRELIMINARY AMENDMENT

Assistant Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

Applicants understand that this application has not yet been examined on the merits. Accordingly, please enter the enclosed amendments and remarks into the application, pursuant to 37 CFR § 1.115(b)(1).

AMENDMENTS

Please delete the current ~~TITLE~~ of the application and replace it with the following:

**PROCESS FOR MAKING HEPATOCYTES  
FROM PLURIPOTENT STEM CELLS**

Please delete the priority information on page 2, lines 13-18, and replace it with the following:

Q' This application is a continuation-in-part of USSN 09/872,182, filed May 31, 2001; and International Patent Application PCT/US01/13471, filed April 26, 2001, which designates the U.S. and was published as WO 01/81549 on November 1, 2001. This application also claims priority to U.S. provisional patent application 60/200,095, filed April 27, 2000. The three priority applications and U.S. utility application 09/718,308 are hereby incorporated herein by reference in their entirety.

Please cancel claims 1-12 without prejudice, and replace them with the following new claims:

- Q<sup>2</sup>
13. A method for producing differentiated cells from primate pluripotent stem (pPS) cells, comprising culturing the pPS cells or their progeny in a medium containing a histone deacetylase inhibitor, until at least ~60% of the cultured cells have at least three of the following characteristics:
- antibody-detectable expression of  $\alpha_1$ -antitrypsin (AAT);
  - antibody-detectable expression of albumin;
  - absence of antibody-detectable expression of  $\alpha$ -fetoprotein;
  - RT-PCR detectable expression of asialoglycoprotein receptor (ASGR);
  - evidence of glycogen storage;
  - evidence of cytochrome p450 activity;
  - evidence of glucose-6-phosphatase activity; or
  - the morphological features of hepatocytes.
14. The method of claim 13, wherein at least about 60% of the cells have at least five of said characteristics.